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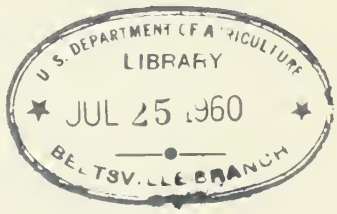
June 1960

Report of Special Meetings on

SCRAPIE

Held During November and December 1959



UNITED STATES DEPARTMENT OF AGRICULTURE

Agricultural Research Service

INTERNATIONAL PANEL OF SCRAPIE SPECIALISTS

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PREFACE

Seven special meetings to discuss technical aspects of scrapie were held during November and December 1959.

These meetings are part of the continuing effort by the Agricultural Research Service to work closely with sheep producers, other industry leaders, disease research and control workers, and special consultants in developing procedures followed in the Cooperative State-Federal Scrapie Eradication Program; and were held as follows:

November 23-24, 1959, at Washington, D. C.; November 29, 1959, at Chicago, Ill., sponsored by the National Wool Growers Association during the International Livestock Exposition to permit the greatest possible participation by sheep producers and the agricultural press; December 2-3, 1959, at Purdue University, Lafayette, Ind.; December 4-5, 1959, at Ohio State University, Columbus, Ohio; December 7-8, 1959, at Denver, Colo.; December 10-11, 1959, Sacramento and Davis, Calif., respectively; December 16, 1959, at San Francisco, Calif., the Panel appeared on the program of the annual meeting of the United States Livestock Sanitary Association.

The State-Federal Cooperative Scrapie Eradication Program is based on principles developed through research conducted in France and Great Britain. Federal and State representatives have visited institutions in these countries to consult with those experienced in scrapie research.

Two of the principal scrapie research institutions in the world are the Agricultural Research Council Field Station, Compton, England, and the Moredum Institute, Edinburgh, Scotland. Drs. W. S. Gordon and J.T. Stamp, respectively, direct these research stations and are recognized to be world authorities on scrapie and other sheep diseases. It was therefore extremely fortunate that they could come to the United States and through these meetings share their broad knowledge of the disease. With this purpose in mind, the meetings were so arranged to make it possible for many interested persons to hear their lectures and discussions, as well as those of Drs. M. S. Shahan, W. J. Hadlow, and J. L. Hourrigan. At the conclusion of the series, each member of the group who had made formal presentations was asked to summarize his remarks. These summaries, together with accompanying tables and illustrations furnished by them, are presented in this report. In some instances the tables represent work not yet completed.

The ARS Animal Disease Eradication Division sincerely appreciates the efforts of all who were instrumental in arranging the meetings and the interest shown by those who attended. This interest was evidenced by active participation in the discussion of the disease and the eradication program. Particular appreciation is extended to the members of the panel.

SYMPTOMS OF SCRAPIE IN SHEEP

Scrapie is a transmissible disease characterized by an unusually long period of incubation--18 to 42 months or more--and a course of 6 weeks to 6 months or longer. In some cases the course of the disease may be of shorter duration; however, unusual cases have shown symptoms for more than a year before death ensued.

The clinical symptoms of scrapie are well known. In the early stages the animal is nervous and apprehensive. There may be slight tremors of the head and neck or thighs and flanks, and grinding of the teeth. These early symptoms may be overlooked. Symptoms are not constant. They may be present at one time and absent at another. Continued close observation of suspect animals is required.

Often one of the early signs is loss of weight and condition in spite of continued good appetite. The wool becomes dry, lusterless, and dead to the touch. The temperature remains normal.

In many cases rubbing is the first sign noticed and often begins in the tailhead and buttocks area. Before the disease runs its course, buttocks, flanks, and sides may be scraped free of wool from scratching against fences, trees, or walls. Some sheep rub their heads as well as other parts of the body. The underlying skin is normal except for damage caused by rubbing.

When a scrapie-infected animal rubs or is manually stimulated, it usually shows the characteristic "scratch reflex" manifested by turning the head with nibbling movements of the lips and licking motions of the tongue, and wiggling of the tail stump. This symptom may be absent in scrapie or may be present in other diseases. The animal appears to enjoy rubbing or being rubbed.

When an infected sheep is disturbed or excited, or has been introduced to an abnormal environment, symptoms may be less apparent. During the course of the disease there is a progressive locomotor incoordination, a tendency to stumble when the animal leaps to clear objects, and a peculiar gait. Infected animals may pull out wool with their teeth and bite at their legs. Other symptoms include convulsive seizures after rough handling, frequent dribbling of urine, impairment of vision, nystagmus, excitability, emaciation, prostration, and finally death. Recovery is extremely rare although some animals may show temporary improvement.

(SUMMARY)

SCRAPIE AND SCRAPIE RESEARCH AT THE BRITISH AGRICULTURAL RESEARCH COUNCIL FIELD STATION COMPTON, BERKSHIRE, ENGLAND

W. S. Gordon

Scrapie is an insidious disease of sheep characterised by a progressive degenerative disorder of the central nervous system accompanied by clinical signs indicative of a sensation of intense irritation of the skin, tremors, and incoordination of gait. Affected animals rarely recover. The disease has been known in Western Europe for over two centuries where it has waxed and waned in different breeds over long periods of years. While the incidence of infection is not usually high, the disease can sometimes cause devastating loss in flocks of purebred sheep, but it is not usually the cause of serious loss in commercial flocks. Scrapie was first diagnosed in the United States in 1947 and it has spread, within one breed, to many States. As a result, an eradication programme was commenced in the United States in 1952. This programme was based on research work carried out in Europe, mainly in Great Britain.

Apart from important scientific reasons for determining the nature of an apparently unique type of transmissible agent there are important practical reasons for learning more about the nature of this disease and its method of spread. Its occurrence has gravely interfered both with national and international sheep trade, and it is to the mutual benefit of the United States, Great Britain, and other countries in which the disease occurs, or may occur, to press on with its investigation.

The Agricultural Research Council Field Station at Compton is particularly suitable for this work since it comprises an estate of 2,000 acres with several farms on which farm and laboratory animals of known health history are produced for the purpose of investigating diseases in farm animals. There is a research institute on the centre of the estate with 26 isolation buildings each capable of accommodating 24 adult cattle. Thus experiments involving 600 to 700 cattle or several thousand sheep, pigs, or goats can be set up as the need arises. The number of animals on the station varies according to the work in progress and at present includes about 1,200 cattle, 24 breeds of sheep in flocks of 30 ewes each, a herd of large white pigs producing about 2,000 annually, 800 goats, and an autosexing flock of poultry. Including laboratory animals there are usually about 30,000 animals all serving experimental needs in one form or another. Hundreds of goats and about 2,000 sheep are involved in scrapie experiments. The staff at Compton has had a long experience in the investigation of this disease and to support its work and keep a flow of animals available for experiment there is a large agricultural enterprise producing as much home grown food as possible to maintain the operation. It would cost about $6,000,000 to match the facilities now available at Compton.

As a result of research work in Britain, certain well-defined facts about scrapie have been established and these may be outlined briefly as follows:-

1. Experimental Transmission of the Disease

It has been proved conclusively that scrapie is an inoculable disease and the transmissible agent can be passed in series, indefinitely, from sheep to sheep with cell-free filtrates prepared from the tissues of infected sheep. This is a characteristic normally associated with the activity of a filterable virus.

2. The Nature of the Transmissible Agent

The transmissible agent can withstand boiling and exposure to concentrations of chemical agents which inactivate all other known viruses. Moreover, the transmissible agent has shown no evidence of producing antibodies despite many attempts by various workers to demonstrate their presence. Further, the lesions of nerve cell degeneration in the brain of affected animals do not resemble those usually associated with a virus infection. The incubation period after inoculation is also peculiar since it is seldom less than 4 months and may extend to 15 months and upwards. Another baffling and very inconvenient characteristic, from the research point of view, is the wide variation in susceptibility to experimental infection not only between different breeds of sheep but also between families within a breed. This difference in susceptibility has not been shown to be due to the presence of antibodies in resistant animals which suggests that the genetic constitution of the animals concerned is an important factor in determining infection. The variation in susceptibility together with the long incubation period has made progress in research, using sheep as experimental animals, slow and frustrating. The fact that the filterable agent of scrapie has some characteristics that differ from those of known filterable viruses has led to much speculation about its true nature, and it is hoped that the work now in progress will ultimately characterise the agent more precisely.

3. The Natural Method of Spread

The natural method of spread of scrapie is the subject of considerable controversy. In countries where the disease is enzootic, it has shown an ability to spread from one pure breed to another. How such spread occurs is a matter for conjecture. It could be by interbreeding when upgrading flocks or it could be by contact between breeds. Great difficulty has been experienced in determining experimentally whether one or both methods are involved. Present evidence clearly favours the view that the disease passes in families from infected parents to some of their offspring. Nevertheless, numerous authors have provided evidence, largely from field observations, that the disease may spread by contact. Under experimental conditions, in which the animals are housed indoors, there has been no recorded instance of spread by contact from diseased to healthy animals. Consequently, it may be concluded that spread within families is probably much more important than spread by contact. However, at Compton we have recently had scrapie develop in a goat that was infected by feeding it with a suspension of brain tissue from an affected animal. The incubation period was 15 months. This animal was in contact

with other cases of scrapie in goats, and therefore may have contracted the disease by contact, and not as a result of the dose administered. However, the incubation period of 15 months is not outwith that normally expected following inoculation. Nevertheless, the fact remains that this is the only case of scrapie that we have observed in a goat in which the animal was not inoculated.

If this observation is confirmed--and we are trying to resolve the issue in both sheep and goats--it would make spread of the disease through ingestion, or by contact, an acceptable possibility.

4. Variation of Susceptibility

In Britain there are 36 different registered breeds of sheep, and at Compton samples of 24 of these breeds have been kept as breeding flocks of approximately 30 ewes each. About 40 animals from each of these flocks have been tested for susceptibility to experimental infection with scrapie. This has demonstrated that there is an astonishingly wide difference in susceptibility among the samples of the various breeds tested, ranging from no affected animals in one breed to as many as 78 percent in another. It was also established that in any one breed some families might be resistant and others susceptible to experimental infection.

This information makes it clear that one must be cautious in assessing the results of scrapie transmission experiments. Not only must the inoculum used be infective but the recipient animals must be susceptible; otherwise, transmission fails. Again this suggests that the genetic constitution of the recipient animal is an important factor in determining infection. The application of this knowledge to experiments in studying the methods of spread of the disease by contact or by any other method is obvious.

5. Transmission of Scrapie, Experimentally, from Parents to Offspring

There is much evidence from field observations that either an infected father or an infected mother may sometimes produce affected offspring. It has been proven at Compton that there is a significant correlation between the susceptibility of mothers and their offspring to experimental infection. This correlation, however, although significant is by no means absolute. The correlation between the susceptibility of fathers and their offspring has not yet been proven experimentally but there is good field evidence that affected rams can sometimes produce affected offspring. When both parents are affected, present evidence suggests that the offspring are more liable to develop the disease. Even here disconcerting results can be obtained as illustrated by the following observation. A ram and a ewe which were the progeny of parents that both died of scrapie were mated and produced three crops of lambs. The ewe and the ram developed scrapie when they were 2 years 8 months and 2 years 10 months old, respectively. The second crop of lambs, a male and a female, both developed scrapie when they were 2-1/2 years old. At this time, the first crop consisting of one male lamb was still apparently normal, however, when he reached the age of 4 years 2 months he developed scrapie. The third crop which was one female born in February 1956 had not shown signs of scrapie up to December 1959 but in January 1960, when almost 4 years old, symptoms of scrapie developed.

In another experiment, a flock of 140 Cheviot ewes and 4 rams were inoculated with the scrapie agent 20 days after they had been mated. Two of the rams and 45 of the ewes developed scrapie. Lambs were born to these inoculated parents when scrapie was prevalent amongst the ewes and of 123 lambs born, 9 developed scrapie when they were 17 to 18 months of age. The mothers of 7 of these lambs died of scrapie, and the mothers of the remaining 2 have remained healthy so far. Unfortunately, it was not known which of the four rams was the sire of the affected lambs, and so another experiment is in progress in which the susceptibility of both parents to experimental infection will be known.

6. Transmission of Scrapie to Goats

It has previously been reported from Compton that scrapie can be transmitted to goats and passed in series indefinitely through these animals. It can also be passed from goats back to sheep again, producing the classical symptoms of scrapie. The indications are that provided scrapie brain is used as inoculum and provided the inoculation is made intracerebrally, the "take" of scrapie in goats will be 100 percent of animals inoculated. This finding will make much work on scrapie, which was hitherto difficult or impossible in sheep, a practicable proposition in goats. Already experimental results indicate that if an inoculum prepared from brain tissue is treated by physical or chemical processes, or if the inoculum is given by a route other than injection into the brain, the "take" of scrapie may be reduced, and the incubation period may be lengthened. It has also been found that the transmissible agent can be detected in the cerebro-spinal fluid 24 hours after experimental infection, and that it can be recovered, as the disease progresses, from the brain, pituitary, adrenal gland, spleen, pancreas, liver, and sciatic nerve in that order.

Further work in progress aims at defining more perfectly the pathology, natural method of spread, immunology, diagnosis, methods of prevention and control or eradication of the disease.

The fact that the spread of scrapie infection in the United States appears to be confined to one breed of sheep suggests that the present eradication programme may be effectively blocking the excursion of infection into other breeds. The elimination of sources of infection in a country in which the disease has comparatively recently made its appearance must surely result in a reduction in the spread of infection. If the programme is relentlessly pursued, and if necessary revised as fresh information dictates, eradication may yet be achieved.

Administration Building, Compton Station England

Harvesting grain at Compton Station, England

Field Station at Compton, England

Bringing feed into isolation compound

Isolation facilities

Isolation facilities

goats and sheep are used at Compton in scrapie research

Experimental sheep are anesthetized prior to intracerebral inoculation

Preparation for intracerebral inoculation

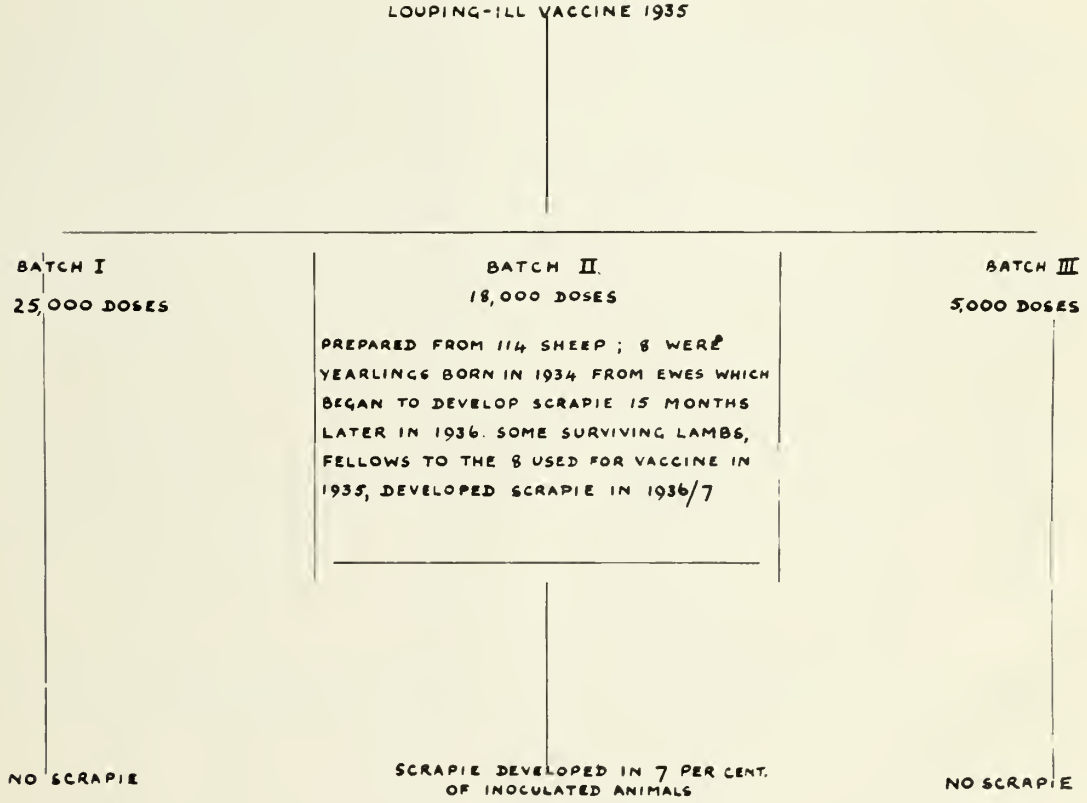
Intracerebral inoculation

Goats used in experiments

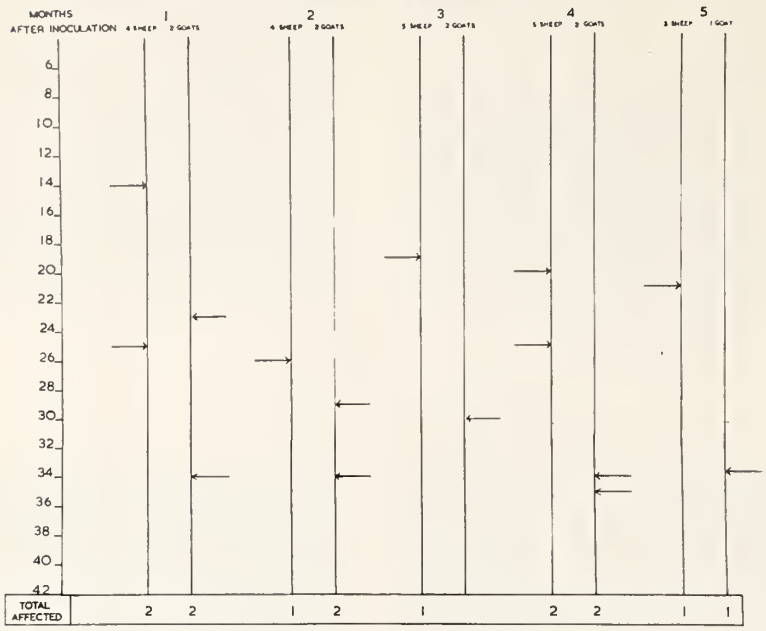
Sheep used in experiments

Summary of Result of Scrapie Transmission Experiment 1938 to 1942

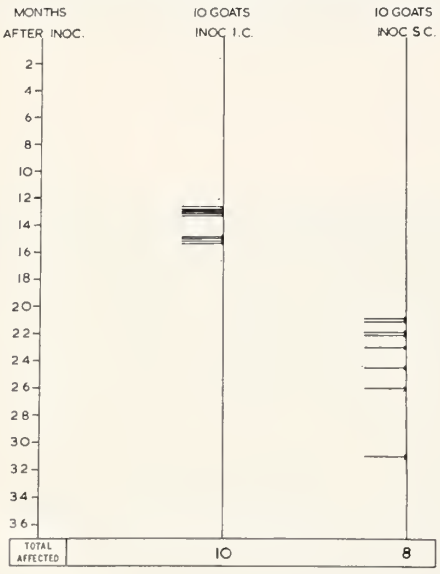
Route of Inoculation	Inoculum	Number of Sheep	Incidence of Scrapie				First case in hme after inocula-tion
			Within two years of inoculation		Up to 4 yrs. 2 months after inoculation		
			Scrapie	Percent	Scrapie	Percent	Months
Subcutaneous	Saline and Broth, equal parts Suspending fluid for all tissues	60	0		5	8	30
	10% Normal Sheep Brain, Cord and Spleen	60	0		3	5	29
	10% Scrapie Brain, Cord and Spleen	60	8	13	22	37	15
	Supernatant Fluid from Centrifuged Scrapie Brain Cord and Spleen 3,000 RPM	60	11	18	25	42	16
	Gradocol membrane Filtrate of above Supernatant Fluid A.P.D. 0.69 ✓	60	4	7	19	32	19
	Scrapie Brain, Cord and Spleen Heated at 60° C for 30 minutes	60	5	8	17	28	18
	Scrapie Brain excluding Medulla 1/5,000,000	10	0		2	20	38
	" " " " 1/50,000	20	1	5	8	40	20
	" " " " 1/50	20	1	5	5	25	19
	" " " " 1/5	20	3	15	0	45	17
	Scrapie Medulla and Cord 1/5,000,000	10	0		9		----
	" " " " 1/50,000	20	0		8	40	29
	" " " " 1/50	19	3	16	6	32	17
	" " " " 1/5	20	7	35	8	40	19
	Scrapie Spleen 1/5,000,000	10	0		2	20	30
	" " 1/50,000	19	0		4	21	28
	" " 1/50	19	1	5	6	32	24
	" " 1/5	20	1	5	5	25	24
Intracerebral	20% Scrapie Brain and Cord	30	13	43	20	67	7
Not inoculated	Controls	30	0		1	3	42
Subcutaneous	10% Scrapie Brain, Cord and Spleen	3 sheep killed each month after inoculation for hiatological examination of medulla. Vacuoles were not observed in the nerve cells until clinical signs were manifest at 21 months.					


LOUPING-ILL VACCINE 1935
BATCH I
25,000 DOSES
NO SCRAPIE
BATCH II.
18,000 DOSES
PREPARED FROM 114 SHEEP ; 8 WERE YEARLINGS BORN IN 1934 FROM EWES WHICH BEGAN TO DEVELOP SCRAPIE 15 MONTHS LATER IN 1936. SOME SURVIVING LAMBS, FELLOWS TO THE 8 USED FOR VACCINE IN 1935, DEVELOPED SCRAPIE IN 1936/7
SCRAPIE DEVELOPED IN 7 PER CENT. OF INOCULATED ANIMALS
BATCH III
5,000 DOSES
NO SCRAPIE

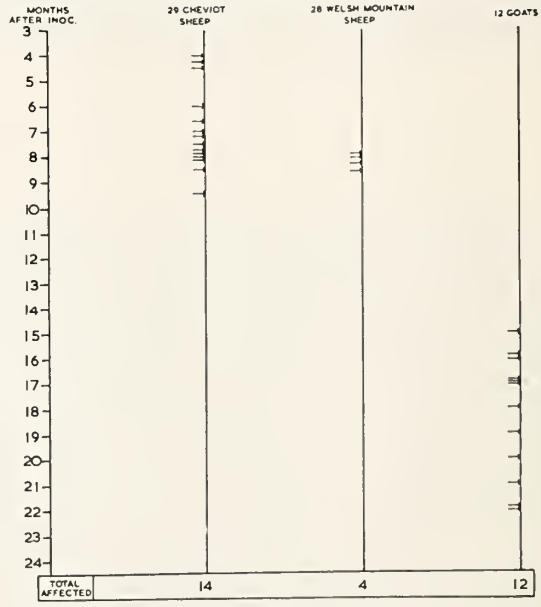
INTRACEREBRAL INOCULATION OF SHEEP AND GOATS ON 27.11.56 WITH BRAIN SUSPENSION FROM FIVE SCRAPIE AFFECTED SWALEDALE SHEEP

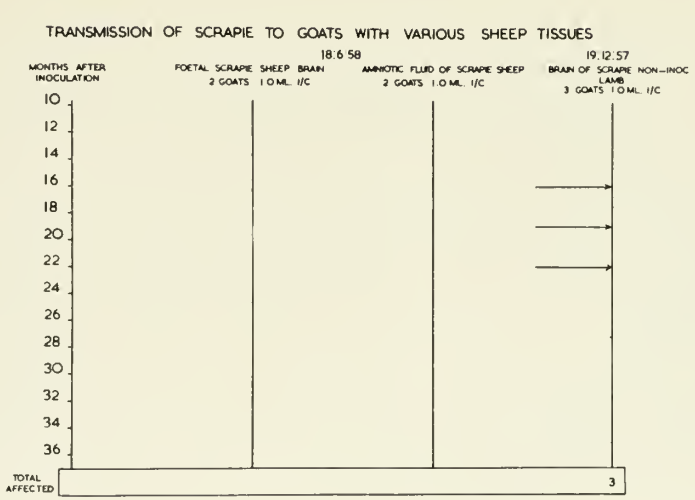


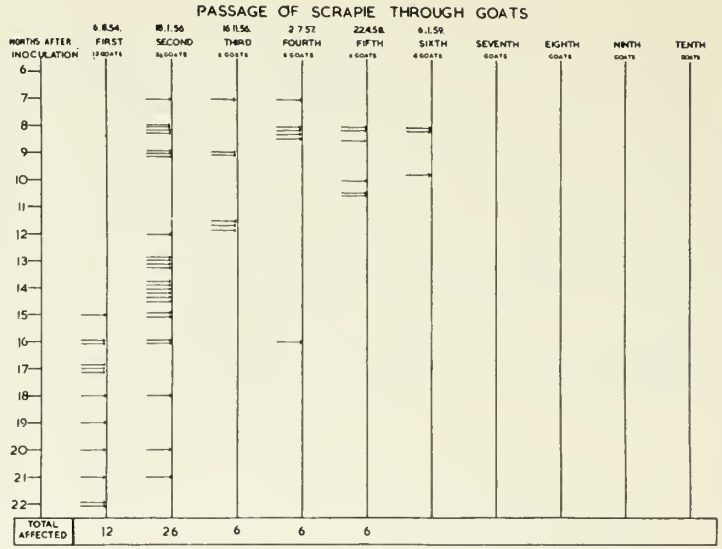
INTRACEREBRAL AND SUBCUTANEOUS INJECTION OF GOATS ON 31.7.56 WITH A MIXED BRAIN SUSPENSION FROM SCRAPIE-AFFECTED GOAT No. 104 S AND SHEEP No. 295 U.

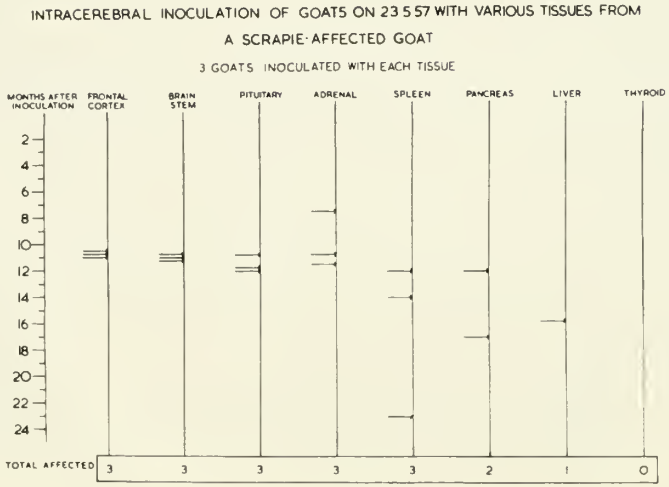


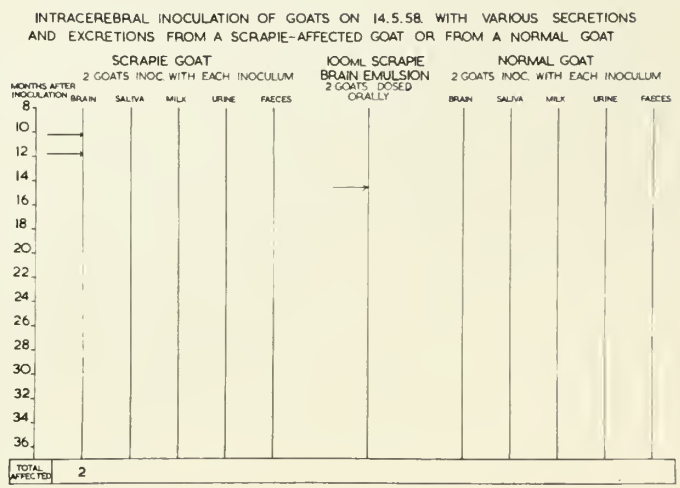
DEVELOPMENT OF SCRAPIE IN 29 CHEVIOT SHEEP, 28 WELSH MOUNTAIN SHEEP AND 12 GOATS INOCULATED INTRACEREBRALLY ON 6.8.54 WITH A 10% BRAIN SUSPENSION FROM A WELSH MOUNTAIN SHEEP



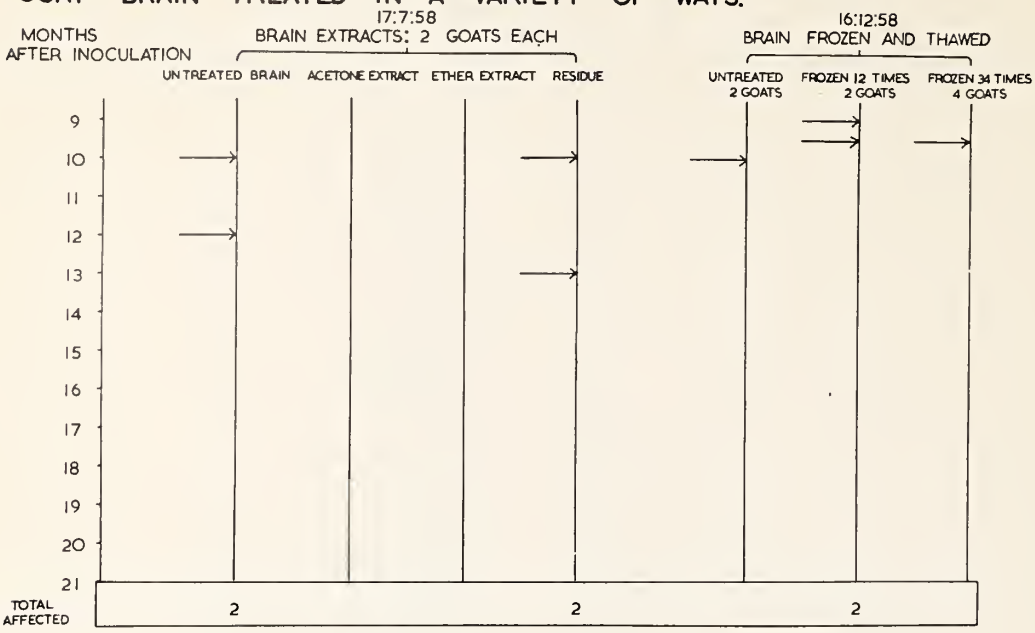

TRANSMISSION OF SCRAPIE TO GOATS WITH VARIOUS SHEEP TISSUES
MONTHS AFTER INOCULATION
18.6.58
FOETAL SCRAPIE SHEEP BRAIN
2 GOATS 1.0 ML. I/C
AMNIOTIC FLUID OF SCRAPIE SHEEP
2 GOATS 1.0 ML. I/C
19.12.57
BRAIN OF SCRAPIE NON-INOC LAMB
3 GOATS 1.0 ML. I/C
10
12
14
16
18
20
22
24
26
28
30
32
34
36
TOTAL AFFECTED
3


PASSAGE OF SCRAPIE THROUGH GOATS
MONTHS AFTER INOCULATION
6.8.54.
FIRST
12 GOATS
18.1.56
SECOND
26 GOATS
16.11.56.
THIRD
6 GOATS
2.7.57
FOURTH
6 GOATS
22.4.58.
FIFTH
6 GOATS
6.1.59.
SIXTH
6 GOATS
SEVENTH
GOATS
EIGHTH
GOATS
NINTH
GOATS
TENTH
GOATS
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
TOTAL AFFECTED
12
26
6
6
6

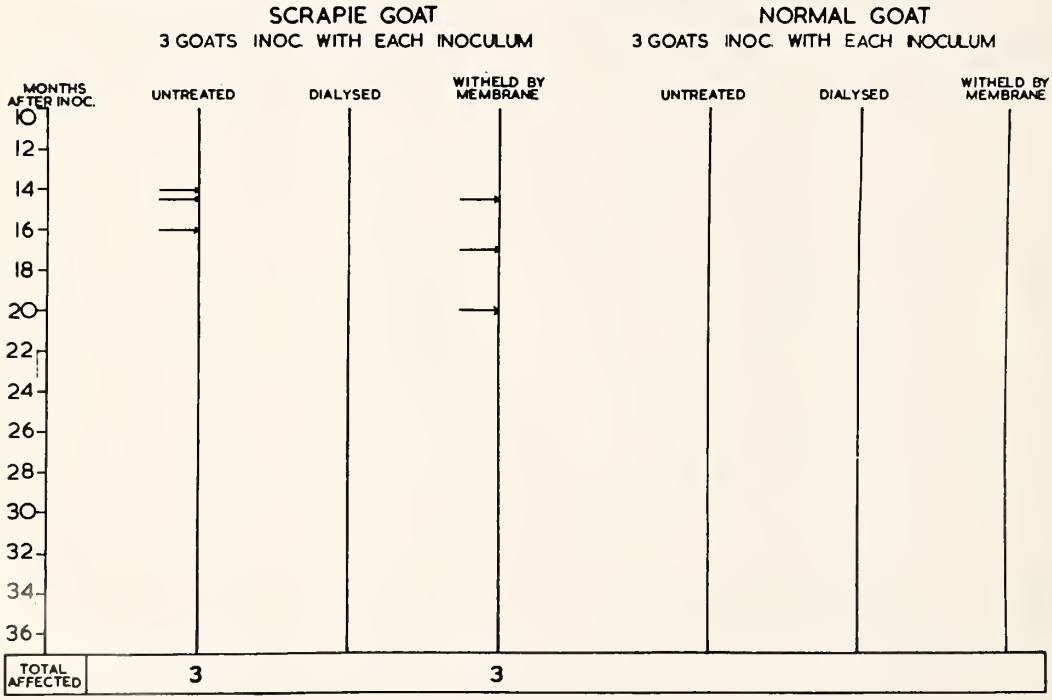

INTRACEREBRAL INOCULATION OF GOATS ON 23.5.57 WITH VARIOUS TISSUES FROM A SCRAPIE-AFFECTED GOAT
3 GOATS INOCULATED WITH EACH TISSUE
MONTHS AFTER INOCULATION
FRONTAL CORTEX
BRAIN STEM
PITUITARY
ADRENAL
SPLEEN
PANCREAS
LIVER
THYROID
2
4
6
8
10
12
14
16
18
20
22
24
TOTAL AFFECTED
3
3
3
3
3
2
1
0


INTRACEREBRAL INOCULATION OF GOATS ON 14.5.58. WITH VARIOUS SECRETIONS AND EXCRETIONS FROM A SCRAPIE-AFFECTED GOAT OR FROM A NORMAL GOAT
SCRAPIE GOAT
2 GOATS INOC. WITH EACH INOCULUM
100ML SCRAPIE BRAIN EMULSION
2 GOATS DOSED ORALLY
NORMAL GOAT
2 GOATS INOC. WITH EACH INOCULUM
MONTHS AFTER INOCULATION
BRAIN
SALIVA
MILK
URINE
FAECES
BRAIN
SALIVA
MILK
URINE
FAECES
8
10
12
14
16
18
20
22
24
26
28
30
32
34
36
TOTAL AFFECTED
2

OCCURRENCE OF SCRAPIE FOLLOWING I.C. INOCULATION OF SCRAPIE GOAT BRAIN TREATED IN A VARIETY OF WAYS.



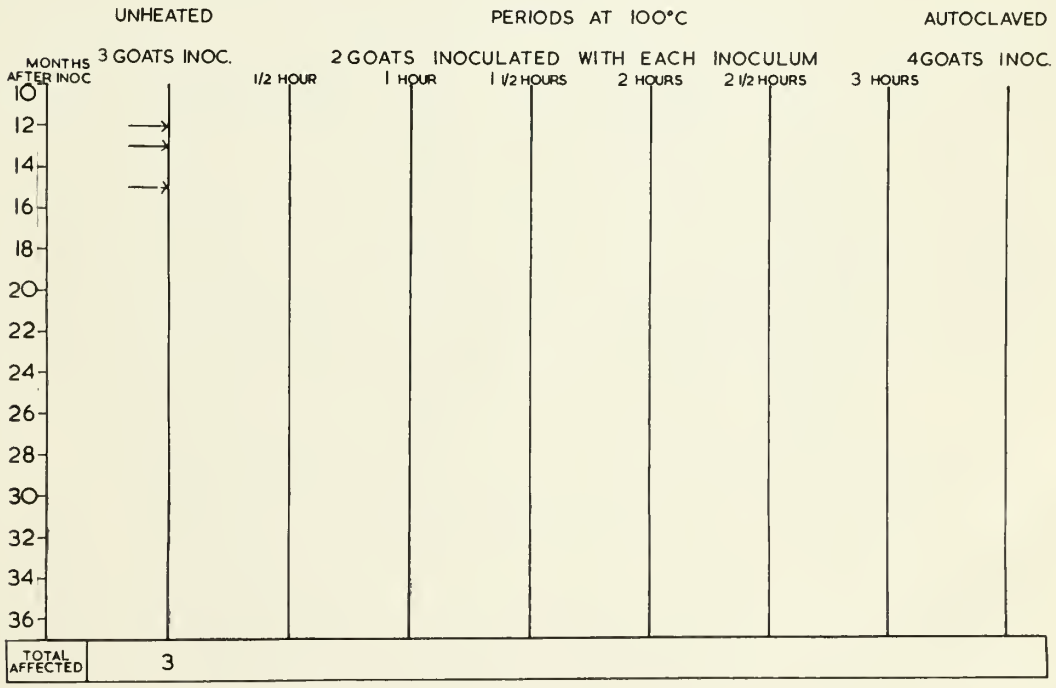
INTRACEREBRAL INOCULATION OF GOATS ON 20·2·58 WITH NON-DIALYSED AND DIALYSED C.S.F. FROM A SCRAPIE AFFECTED GOAT OR FROM A NORMAL GOAT



SUBINOCULATIONS OF VARIOUS TISSUES FROM DONOR GOATS INOCULATED I.C. ON 3·6·58 WITH SCRAPIE GOAT BRAIN SUSPENSION

DONOR NUMBER	KILLED/ DAYS AFTER INOC.	DATE	SYMPTOMS OF SCRAPIE	APPEARANCE OF SCRAPIE IN RECIPIENT GOAT INOCULATED WITH:-								
				BLOOD	C.S.F.	URINE	BRAIN	SCIATIC NERVE	PITUITARY	ADRENAL	MUSCLE	SALIVARY GLAND
C94	1	4·6·58	NO		495 DAYS				461 DAYS			
C7	8	11·6·58	NO				365 DAYS					
C10	15	18·6·58	NO		376 DAYS		344 DAYS					
C12	22	25·6·58	NO				323 DAYS					
C8	36	9·7·58	NO				323 DAYS		336 DAYS			
C72	56	29·7·58	NO				342 DAYS					
C70	92	3·9·58	NO						316 DAYS			
W327	121	2·10·58	NO		341 DAYS		260 DAYS	354 DAYS	241 DAYS			
C9	147	30·10·58	NO				232 DAYS		323 DAYS			
C11	176	26·11·58	NO		306 DAYS		222 DAYS		264 DAYS			
C76	217	7·1·59	NO						266 DAYS			
C64	243	2·2·59	YES				224 DAYS					
C54	279	10·3·59	YES		DIED NOT SCRAPIE 211 DAYS							
C157	344	13·5·59	YES									

INTRACEREBRAL INOCULATION OF GOATS ON 21·5·58 WITH HEATED OR UNHEATED C.S.F. FROM A SCRAPIE AFFECTED GOAT



OCCURRENCE OF SCRAPIE IN THE PROGENY OF INOCULATED PARENTS

PARENTS

INOCULUM	EWES	RAMS
10% SCRAPIE BRAIN SUSPENSION IN SALINE	140	4
AFFECTED WITH SCRAPIE	45	2

OFFSPRING

TOTAL BORN	59	64
AFFECTED WITH SCRAPIE	7	2

COMPARATIVE SUSCEPTIBILITY TO SCRAPIE OF 24 DIFFERENT BREEDS OF SHEEP
INOCULUM: 10% SUSPENSION OF SCRAPIE BRAIN TISSUE IN SALINE

BREED	NUMBER INOCULATED	AFFECTED with SCRAPIE	PERCENT
HERDWICK	36	28	78
DALESBRED	43	31	72
SWALEDALE	46	25	54
S.S. CHEVIOT	45	16	36
DERBY GRITSTONE	46	16	35
EXMOOR HORN	41	14	34
BORDER LEICESTER	42	11	26
SCOTTISH BLACKFACE	44	8	18
SOUTH DEVON	35	6	17
ROMNEY MARSH	43	7	16
WELSH CHEVIOT	40	6	15
RYELAND	34	5	15

BREED	NUMBER INOCULATED	AFFECTED with SCRAPIE	PERCENT
DORSET HORN	45	6	13
SUFFOLK	51	6	12
LEICESTER	42	5	12
WELSH MOUNTAIN	42	4	10
HAMPSHIRE DOWN	30	3	10
N. S. CHEVIOT	45	4	9
SOUTHDOWN	38	3	8
WILTSHIRE HORN	57	4	7
SHROPSHIRE	41	2	5
KERRY HILL	41	1	2
CLUN FOREST	52	1	2
DORSET DOWN	48	0	0

INCUBATION PERIODS FROM TIME OF INOCULATION RANGED FROM 3½ TO 23 MONTHS
PERIOD OF TEST: JULY 1957 TO JULY 1959

(SUMMARY)

SCRAPIE AND SCRAPIE RESEARCH AT ANIMAL DISEASES RESEARCH ASSOCIATION, MOREDUN INSTITUTE, EDINBURGH, SCOTLAND

J. T. Stamp

Scrapie disease of sheep has been present in Great Britain and Western Europe for more than two centuries. At the present time, it does not give rise to valuable losses among our flocks as a whole, but from time to time it has presented a serious problem to individual flockmasters. One of its important effects has been its interference with the export trade in pedigree sheep from Great Britain to Canada and the United States where the disease is thought to have made its appearance within recent years. This is unfortunate for both Britain and America. For the former it means a considerable loss of national prestige since Britain regards herself as being unrivaled in the breeding of good sheep while sheep breeders of the United States on occasion desire to import British blood lines.

Unfortunately, this resume does not answer the scrapie problem, but it does set forth the research work that has been carried out by scientific workers at the Moredun Research Institute, Edinburgh, Scotland.

Some facts are indisputable. In the first place, scrapie can be made to occur in Cheviot and Scottish Blackface sheep when brain, spleen, and lymph glands taken from sheep affected with scrapie are inoculated either intracerebrally, subcutaneously, or intradermally. The disease occurs 5 months or more after inoculation. Further, it is known that Cheviot lambs develop the disease before they are 9 months of age if they are inoculated at birth. This is at an age when natural scrapie never occurs. On the other hand, similar sheep inoculated with brain tissue taken from normal sheep failed to develop the disease except on one occasion.

The scrapie agent has also been successfully passaged blindly at 2 month intervals through seven groups of Cheviot sheep; therefore, it would appear that the agent is self-replicating. The results of dilution and filtration experiments are also consistent with what one might expect with a biologically active particulate agent such as a virus. One feature of the Moredun experiments with sheep is that the incidence of the experimental disease is always low, averaging about 27 percent. Only on one occasion has the incidence been 100 percent and that was when the inoculated sheep were the offspring of a scrapied ram.

However, there is some evidence which might suggest that the scrapie agent is not a virus, at least not one of the kind presently recognized. It is beyond dispute that the disease can still be reproduced experimentally in series when the agent has been boiled at 100° C. for 8 hours or heated at 96° C. for 24 hours, and that the heated fraction is self-replicating. Equally clear is the fact that the transmissible factor is present in about equal quantity in both boiled and unboiled suspensions. In addition to being highly resistant to heat, it is known that the agent can withstand

the action of 3 percent formalin for 13 days at 37° C. or 0.8 percent formalin at 4° C. for 4 months. The agent is also resistant to the action of acetylethyleneimine, known to destroy nucleoprotein. It will not withstand autoclaving at 20 lbs. per square inch pressure for 30 minutes which develops a temperature of 127° C. Attempts to purify and concentrate the scrapie agent by butyl alcohol fractionation at various PH ranges followed by centrifugation were not successful since the agent was present at all PH ranges from 4.5 to 9 in both the gel and aqueous phases.

It can be seen that the evidence as to the etiology of scrapie is difficult to interpret. On the one hand, the results of transmission experiments suggest that scrapie is an infectious disease caused by a virus whereas the resistance of the agent to heat and chemicals make it appear unlikely to be a typical virus particle.

Numerous unsuccessful attempts have been made to reproduce scrapie in the mouse, the rat, and the guinea pig, and to grow the agent in tissue culture. In addition no evidence of antigen or antibody has been found nor have electromicroscopic observations revealed any virus particles in scrapie brain or spleen.

In view of these contradictory findings, a breeding experiment was begun in 1955 by establishing a "dirty" flock consisting of the immediate offspring of scrapied rams or ewes and establishing a second flock of "clean" sheep. The experiment was designed to determine if the disease is familial and if so to provide information on the mode of transmission since a knowledge of the epidemiology of the disease is essential for rational field control. Lambs from four mating groups (viz. 1. Clean rams crossed with clean ewes; 2. Dirty rams crossed with clean ewes; 3. Dirty rams crossed with dirty ewes; and 4. Clean rams crossed with dirty ewes) have been produced and it would seem that if the parent had scrapie, the chances of its offspring having scrapie are relatively high. Although the incidence would appear to be higher in the offspring of scrapied dams than of scrapied sires, this is probably due to unbalanced representations in the early years of the experiments. Satisfactory evidence regarding the sire should be available during 1960 when numerous offspring of scrapied sires out of clean dams reach the age when scrapie can be expected to occur. Mixed semen and egg transplantation experiments will further elucidate this point when the offspring mature. It could, of course, be argued that the above familial association was apparent rather than real due to the offspring being raised in a scrapie environment; however, in a control contact experiment using scrapie-free sheep, similar offspring to the above have been left continuously exposed to scrapied sheep over the same period of time and have so far remained free of the disease. Similarly, 100 Cheviot sheep left in continuous contact with numerous scrapied sheep over a 5-year period also remained free of the disease. In this case the contact sheep did not breed. These findings are, so far as they have gone, in contradiction to the experimental evidence of Greig who claimed that scrapie could be transmitted through soil or pasture. Our experiments are, however, far from complete.

Considerable work on the pathology of scrapie has shown that the characteristic and most consistent lesions are in the neurons of the brain stem and cerebellum although astrocytic proliferation is also seen. All the neuronal lesions consist of various stages of degeneration and/or vacuolation of the cytoplasm. The medulla and pons are the most suitable parts of the central nervous system for diagnostic

examination. The lesions in the medulla can be found in any of the cell groups or nuclei, but the following nuclei are more commonly affected than others:

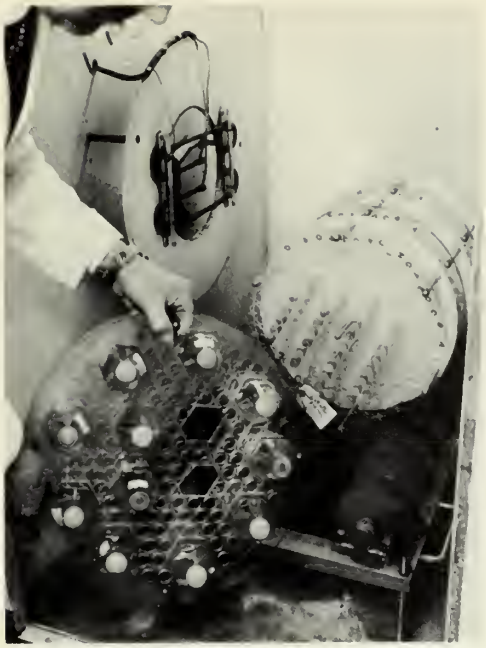
1. Arcuate
2. Raphe
3. Reticular
4. Dorsal motor vagus
5. Cuneate
6. Red nucleus

The numerical difference in the incidence of vacuolated neurons between scrapied animals and apparently healthy sheep is very obvious when serial sections of the medulla are examined.

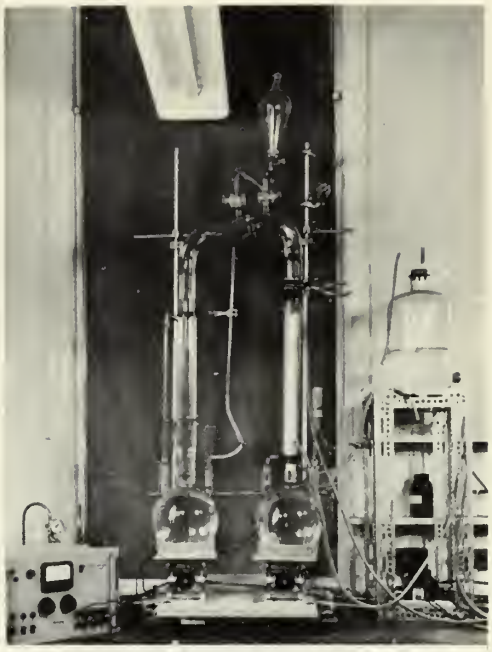
No evidence could be obtained that muscle lesions are a characteristic finding in scrapie.

Some of the Administration buildings, sheep barns, and pastures at Moredun Institute, Gilmerton, Edinburgh, Scotland

Crossbreeding experiments and contact experiments under way



Tissue culture studies

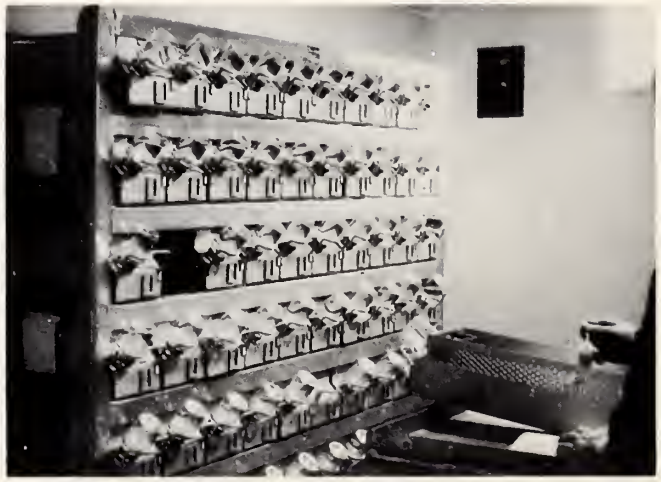


Electrophoresis apparatus

High-speed centrifuge

Part of freeze-drying apparatus

View of cold laboratory



Mouse colony

ROUTES OF INOCULATION - (USING SCRAPIE SHEEP C.N.S.)

ROUTE	NO. OF CASES	NO. INOC.	NOTES
SUBCUTANEOUS	7	20	
	2	5	
	4	10	
	9	30	
	8	20	
	3	15	
	3	15	
	10	10	BORDER LEICESTER
INTRADERMAL	1	2	
	2	5	

TISSUES TESTED - (OTHER THAN SCRAPIE SHEEP C.N.S.)

ROUTE OF INOCULATION IS INTRACEREBRAL, UNLESS OTHERWISE STATED

TISSUE	NO. OF CASES	NO. INOC.	NOTES
1ST TISSUE POOL	6	10	LYMPH GLANDS, SPLEEN & SKIN
	3	9	LYMPH GLANDS, SPLEEN & SKIN S.C.
2ND TISSUE POOL	1	10	LYMPH GLANDS, SPLEEN & SKIN
SPLEEN	3	9	AS USED IN 1ST TISSUE POOL
CEREBRO-SPINAL FLUID	3	9	
LYMPH GLANDS	2	9	AS USED IN 1ST TISSUE POOL

ROUTES OF INOCULATION - (USING SCRAPIE SHEEP C.N.S.)

ROUTE	NO. OF CASES	NO. INOC.	NOTES
INTRACEREBRAL	0	10	BLACKFACE LAMBS
	6	15	CHEVIOT LAMBS
	11	14	CHEVIOT LAMBS
	6	20	
	4	10	10^{-3} DILUTION
	3	10	
	6	17	
	5	10	
	6	10	FREEZE-DRIED
	3	20	CHEVIOT LAMBS
	0	26	SUFFOLKS INOC. WITH STRAIN 2
	2	2	SWALEDALES INOC. WITH STRAIN 2
	2	2	X SUFFOLKS INOC. WITH STRAIN 2
INTRACEREBRAL - BLIND PASSAGE 2-MONTHLY INTERVALS 6TH PASS.	3	20	

PHYSICAL TREATMENTS OF SCRAPIE SHEEP C.N.S.

ROUTE OF INOCULATION IS INTRACEREBRAL, UNLESS OTHERWISE STATED

TREATMENT	NO. OF CASES	NO. INOC.	NOTES
HEAT			
AUTOCLAVING 20 LBS. 30 MINS.	0	17	
	0	15	
	0	30	
BOILING FOR 30 MINS.	2	20	
	3	17	
	2	17	
	2	15	LAMBS
	7	50	BOILED SCR. CNS + UNBOILED NORMAL CNS (LAMBS)
	6	50	BOILED SCR. CNS + BOILED NORMAL CNS (LAMBS)
	2	9	
	2	8	
	3	11	SUBCUTANEOUS
DILUTIONS	6	19	10^{-1}
	1	20	10^{-2}
	1	20	10^{-3}
	8	29	BOILED PASSAGE (2ND)
BOILING FOR 8 HRS.	1	21	

PHYSICAL TREATMENTS OF SCRAPIE SHEEP C.N.S.

ROUTE OF INOCULATION IS INTRACEREBRAL, UNLESS OTHERWISE STATED

TREATMENT	NO. OF CASES	NO. INOC.	NOTES
DILUTION			
10^{-1}	2	3	
10^{-2}	0	5	
10^{-3}	0	5	
10^{-4}	0	5	
10^{-5}	3	5	
10^{-1}	6	15	
10^{-3}	4	10	
10^{-5}	1	10	
10^{-7}	0	10	
10^{-9}	0	10	
10^{-1}	0	4	NEUTRALISATION TEST USING NATURAL SCRAPIE SERUM
10^{-2}	1	5	
10^{-3}	0	5	
10^{-4}	0	5	
10^{-5}	1	5	

PHYSICAL TREATMENTS OF SCRAPIE SHEEP C.N.S.

ROUTE OF INOCULATION IS INTRACEREBRAL, UNLESS OTHERWISE STATED

TREATMENT	NO. OF CASES	NO. INOC.	NOTES
FREEZING			
-70°C. FOR 2 MONTHS	4	10	
-40°C. FOR 2 MONTHS	6	10	
	2	10	
-30°C. FOR 20 MONTHS	3	11	BOILED BEFORE INOC.
-30°C. FOR 17 MONTHS	3	20	
-20°C. FOR 2 MONTHS	3	10	
DRYING			
4°C. IN DESICCATOR OVER $CaCl_2$ 2½ YRS.	3	4	

PHYSICAL TREATMENTS OF SCRAPIE SHEEP C.N.S.

ROUTE OF INOCULATION IS INTRACEREBRAL, UNLESS OTHERWISE STATED

TREATMENT	NO. OF CASES	NO. INOC.
FILTRATION - GRADOCOL MEMBRANES		
650 mμ	10	36
420 mμ	3	4
410 mμ	7	29
210 mμ	1	4

CHEMICAL TREATMENTS OF SCRAPIE SHEEP C.N.S.
ROUTE OF INOCULATION IS INTRACEREBRAL, UNLESS OTHERWISE STATED

TREATMENT	NO. OF CASES	NO. INOC.
FORMALIN		
3% AT 37°C. FOR 13 DAYS	5	10
1.5% AT 37°C. FOR 14 DAYS	1	12
0.8% AT 4°C. FOR 2 MONTHS	3	9
0.8% AT 4°C. FOR 4 MONTHS	4	15
FORMALIN 1% & ETHER 1%		
37°C. FOR 14 DAYS	4	12
CHLOROFORM		
5% AT 37°C. FOR 13 DAYS	2	10
1% AT 37°C. FOR 14 DAYS	3	12
PHENOL		
2% AT 37°C. FOR 13 DAYS	3	11
1% AT 37°C. FOR 13 DAYS	3	11

TREATMENT	NO. OF CASES	NO. INOC.	NOTES
ETHER (SOXHLET EXTRACTION)			
EXTRACT	3	15	32-36°C. FOR 10½ HRS.
RESIDUE	5	15	
WATER (SOXHLET EXTRACTION) ON ABOVE ETHER RESIDUE.			
EXTRACT	3	15	FREEZE-DRIED AND RESUSPENDED FOR INOC.
RESIDUE	4	15	94-98°C. FOR 24 HRS.
ACETYLETHYLENEIMINE (Weston Hurst)	3	15	FREEZE-DRIED AFTER TREATMENT

TREATMENT	NO. OF CASES	NO. INOC.
BUTYL ALCOHOL FRACTIONS		
CENTRIFUGED AQUEOUS PHASE pH 9.0	7	15
" " " pH 7.0	9	15
" " " pH 7.0	3	15
" " " pH 4.5	7	15
GEL PHASE pH 4.5	5	15
" " pH 7.0	9	15

Apparently Healthy Sheep

Serial No	No. of Vacuoles in 18 Serial Sections of Parts of the Brain Stem.				Total No. of vacuoles in 54 sections of the whole medulla.	Average No. of vacuoles per section of the medulla.	Various Stages of neurone degeneration	Necrosis of neurones.	Increased perineuronal satellitosis.
	Pons	Medulla Block "A"	Medulla Block "B"	Medulla Block "C"					
1	—	3	—	38	41	0·76	—	—	+
2	—	4	1	52	57	1·05	—	—	+
3	—	—	—	—	—	—	—	—	—
4	—	6	4	—	10	0·18	—	—	—
5	—	6	4	—	10	0·18	—	—	—
6	—	—	—	3	3	0·05	—	—	—
7	—	—	10	4	14	0·26	—	—	+
8	—	—	—	—	—	—	—	—	—
9	—	—	—	—	—	—	—	—	—
10	—	—	4	12	16	0·3	—	—	+

+ = slight.

Clinical Scrapie — Non-advanced

Serial No	No. of Vacuoles in 18 Serial Sections of Parts of the Brain Stem.				Total No. of vacuoles in 54 sections of the whole medulla.	Average No. of vacuoles per section in the medulla	Various Stages of neurone degeneration.	Necrosis of neurones.	Increased perineuronal satellitosis.
	Pons	Medulla Block "A"	Medulla Block "B"	Medulla Block "C"					
11	—	161	1170	450	1781	33	+ +	+	—
12	55	57	53	325	435	8	+	+	+ + + +
13	1060	103	1337	1530	2970	55	+	+	+
14	234	321	356	763	1440	27	+ +	+	+
15	75	270	506	415	1191	22	+ + +	+ + +	—
16	73	197	453	1024	1674	31	+	+	+ +
17	526	57	142	287	486	9	+ + +	+ + +	+
18	234	234	554	634	1422	26	+ +	+	+
19	58	108	390	420	918	17	+	+	+
20	90	252	215	379	846	16	+ +	+	—

+ = slight + + + = severe

+ + = moderate + + + + = very severe

Clinical Scrapie — Advanced

Serial No.	No. of Vacuoles in 18 Serial Sections of parts of the Brain Stem.				Total No. of vacuoles in 54 sections of the whole medulla.	Average No. of vacuoles per section in the medulla.	Various stages of neurone degeneration.	Necrosis of neurones.	Increased perineuronal satellitosis.
	Pons	Medulla Block "A"	Medulla Block "B"	Medulla Block "C"					
21	396	288	393	504	1185	22	+ + +	+ +	—
22	—	1008	180	648	1836	34	+ + +	+	+
23	306	270	288	918	1476	27	+ + +	+ + +	—
24	108	162	972	918	2052	38	+ + +	+ +	+
25	1134	522	1368	1404	3294	61	+ + +	+ +	—
26	324	738	1224	3870	5832	108	+ + + +	+ + + +	+ + +
27	179	522	342	396	1260	23	+ +	+	+ + +
28	1535	450	1440	1584	3474	64	+ +	+	+
29	305	126	776	412	1314	24	+ +	+	+ + +
30	1781	917	1135	2214	4266	79	+ + + +	+ + + +	+ + +

+ = slight + + + = severe

+ + = moderate + + + + = very severe

(SUMMARY)

PATHOLOGY OF SCRAPIE IN GOATS

W. J. Hadlow

In supporting established research on scrapie, the Agricultural Research Service, United States Department of Agriculture, assigned a veterinary pathologist to work with the staff at the Agricultural Research Council Field Station, Compton, Berkshire, England, to help extend the investigation of the pathologic nature of the disease. The study, which has been in progress for the past 22 months, has been concerned primarily with determining the anatomical basis for the syndrome--an aspect hitherto not completely understood. In an effort to clarify the situation, about 40 experimentally affected goats were subjected to detailed clinicopathologic study.

Observations to date indicate that clinically the experimental disease in the goat is essentially like scrapie in the sheep. Onset almost always is gradual after a long incubation period, usually 8 to 15 months. The disease is characterized initially by changes in temperament; the animals become apprehensive and hyperexcitable. Scratching and rubbing of the skin may be observed. This aspect of the disease, which also is apparent early in its course, varies in severity and is not constant. However, insidiously progressive motor disturbances leading to inability to walk or stand invariably ensue as an integral feature of the disease. Tremor, particularly of the head, frequently is seen. In advanced stages, vision becomes impaired, and the goats often acquire a somnolent or demented attitude. Complete prostration unaccompanied by true paralysis supervenes terminally; death usually occurs 3 to 6 months after onset. Animals that are more acutely affected may die within 2 to 3 weeks after the rather abrupt appearance of signs of neurologic disease.

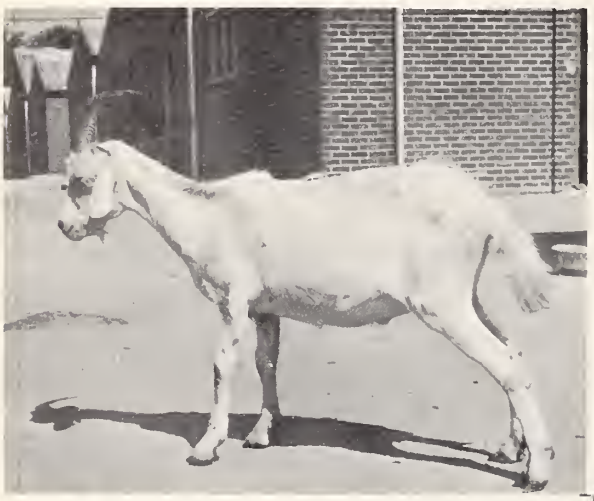
Extensive post-mortem examination of affected goats has revealed significant pathologic changes only in the central nervous system. Microscopically, widespread, essentially nonspecific, degeneration of nerve cells is the principal alteration. Affected neurons are shrunken, deeply basophilic, and may be vacuolated. In some areas nerve cells disappear. These rather subtle regressive changes are accompanied by pronounced astrocytosis--an increase in size and number of astrocytes, the cells which form much of the framework of nervous tissue. When severe, the degenerative changes may result in spongy disintegration of affected gray matter. Loss of myelin is not a feature of the lesion, and acute alterations, including inflammatory changes, are never conspicuous at any time during the course of the disease.

As in any disease of the central nervous system, the distribution of the essential lesion is of particular significance. Although recognizable damage to nerve cells may be widespread, certain parts of the brain characteristically are more regularly and more severely affected than others. Included in this category are such functionally

complex structures as the basal ganglia, thalamus, subthalamus, cerebellum, and midbrain. The medulla oblongata, pons, and spinal cord are less prominently affected. By contrast the cerebral cortex, cerebrospinal ganglia, and spinal nerve roots apparently are not involved. Because little is known about the neurophysiology of the goat or sheep, specific correlation of these anatomical changes with individual clinical signs is not possible at this time. However, in general the pattern of brain damage would seem to explain many typical features of the disease. Much remains to be learned about functional disturbances in the nervous system of an animal affected with scrapie.

In view of the observations presented herein, scrapie can be regarded as a progressive degenerative disorder of the central nervous system; it is not a primary disease of the skeletal musculature as some workers have contended. The fundamental metabolic disturbance responsible for the anatomical changes demonstrated in the nervous tissue remains to be elucidated.

Experimental Scrapie in Goats

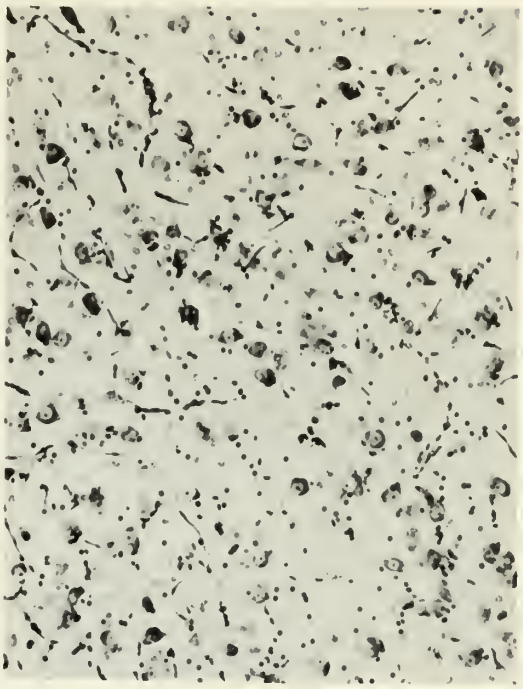


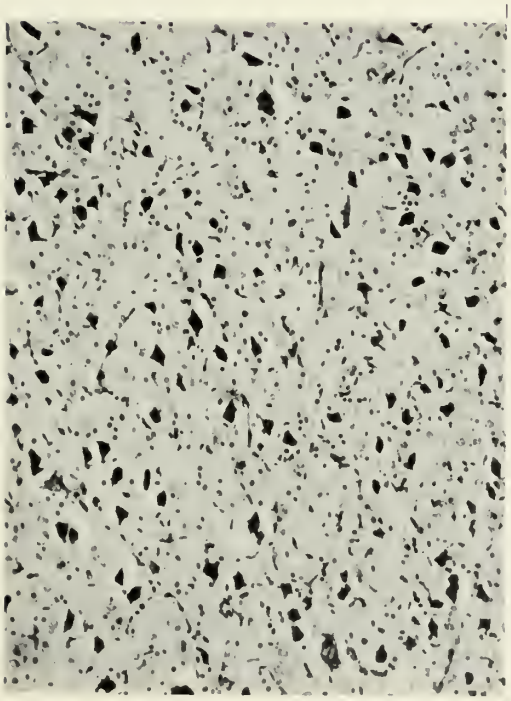
This animal had been showing symptoms for about 3 months. (Note bare patches of skin produced by considerable rubbing and scratching.)

This animal had been showing symptoms for about 2½ months. Little evidence of scratching or rubbing was observed. Animal had an unsteady gait. (Note typical somnolent attitude and drooping ears.)

PHOTOMICROGRAPHS OF LATERAL GENICULATE
(Azure-Eosinate Stain)

Normal goat.

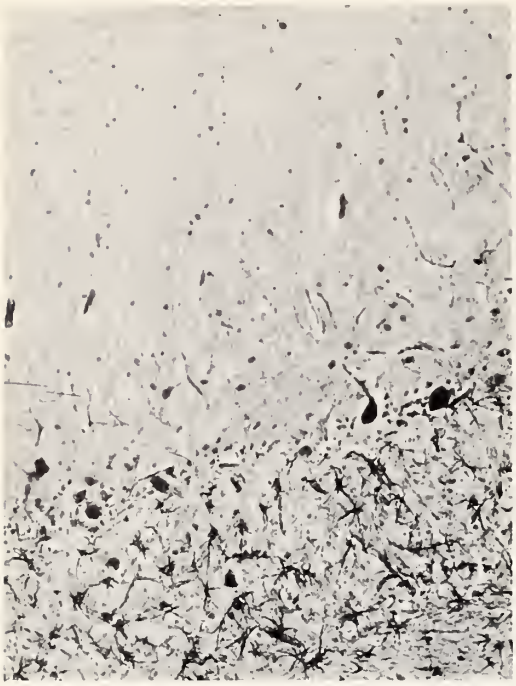




Goat affected with scrapie. Characteristic degenerative changes consist of shrunken, deeply stained nerve cells and an increase in number of astrocytes.

PHOTOMICROGRAPHS OF CEREBELLAR CORTEX

(Cajal's Gold Sublimate Stain)



Normal goat. (Note size and number of astrocytes in granular layer shown at bottom half of photo.)

Goat affected with scrapie. (Note great increase in size and number of astrocytes in granular layer (bottom of photo) and proliferation of glial fibers in molecular layer (top of photo).)

(SUMMARY)

SCRAPIE ERADICATION

J. L. Hourrigan

Reports of Scrapie Outbreaks in the United States

In this country 88 infected flocks have been reported in 73 counties in the following 23 States: Alabama (2), California (8), Connecticut (2), Georgia (1), Illinois (15), Indiana (23), Iowa (1), Kentucky (1), Maryland (1), Michigan (2), Mississippi (1), Missouri (1), New York (3), North Carolina (2), Ohio (12), Oregon (3), Tennessee (2), Texas (1), Utah (1), Virginia (1), West Virginia (1), Wisconsin (2), and Wyoming (2).

The first report of scrapie was from Michigan in 1947. No additional outbreaks were reported until fiscal year 1953 when 10 were disclosed. There were 3 in 1954; 11 in 1955; 23 in 1956; 12 in 1957; 7 in 1958; 11 in 1959; and 10 to date in fiscal year 1960.

The Cooperative Scrapie Eradication Program

The cooperative eradication program is based on procedures long used to eradicate other diseases, with modifications required by the unusual nature of scrapie.

Widespread dissemination of information about the disease and prompt reporting of suspicious cases are stressed.

Tentative clinical diagnosis is confirmed by histopathological studies of brain tissues. The laboratory confirmation is based upon proven research findings. Suspect animals are maintained under observation and are not slaughtered until symptoms develop fully.

Infected flocks and source flocks are quarantined. All sheep and goats in such flocks are slaughtered under supervision at authorized slaughtering plants. Exposed animals moved from these flocks and their immediate progeny are slaughtered also. The premises and vehicles involved are cleaned and disinfected.

Indemnities for slaughtered animals are paid in accordance with State and Federal regulations. Federal indemnity was increased in 1954. It does not exceed 50 percent of the difference between appraised and net salvage value of each animal and is limited to $25 a head for grade and $75 a head for purebred animals. The amount of State indemnity paid is governed by State policy and regulation.

Flocks from which exposed sheep and/or their immediate progeny are removed are inspected at least every 6 months for 42 months to determine if scrapie has been introduced.

Principles of Eradication

The objectives of the Scrapie Eradication Program are control, prevention, and eradication of scrapie.

Only two basic disease eradication principles are applicable in attaining these goals. These are preventing exposure of susceptible animals and increasing their resistance.

Research efforts to produce a vaccine to increase resistance have been discouraging. If either breed or individual animal resistance exists, it might be possible to develop strains of scrapie-resistant sheep. Even if possible, this would be a very long and laborious undertaking.

Preventing exposure of susceptible sheep is the only presently known method of avoiding additional outbreaks. Until research proves conclusively whether scrapie spreads from parent to offspring, or by some form of contact, any effective program must follow appropriately modified conventional methods which embrace both possibilities of spread.

Since the agent is known to exist in visibly affected sheep, it is clear that they must be destroyed. There is no diagnostic test for the disease in an animal not showing symptoms; consequently, there is no way of knowing how many exposed animals may harbor the infectious agent. This factor, linked with the long incubation period, necessitates the slaughter of all exposed animals.

Development of the Eradication Program

Following the first outbreak which occurred in Michigan in 1947, scrapie was again reported in October 1952 when, in two related California outbreaks, 21 sheep were found to be showing symptoms of the disease. The United States Livestock Sanitary Association urged the Department of Agriculture to take immediate action to eradicate scrapie. On October 31, 1952, the Secretary of Agriculture declared an emergency thus providing the means for establishing the Scrapie Eradication Program.

Like all animal disease eradication programs in the United States, it is a State-Federal cooperative program with each agency having certain basic responsibilities.

Regulatory officials recognized scrapie as a particularly difficult disease to combat. It was essential that program procedures be both effective and practical. In developing these procedures, industry representatives and research workers were consulted and all available literature and other information concerning scrapie carefully studied. The program adopted in 1952 was quite similar to the one now being followed.

All sheep in the two California flocks and all exposed sheep moved from them were slaughtered as were the immediate progeny of the movements. The 55 premises involved were cleaned and disinfected. This procedure worked quite well, and now more than 7 years have passed with no extension of infection from these outbreaks. California has since suffered six additional outbreaks. These were not associated with those in 1952. The source of the earlier outbreaks is believed to have been a Canadian flock.

The disease struck next in Ohio where, in fiscal year 1953, five infected flocks were found. The eradication program in Ohio included slaughter of infected flocks but not exposed sheep moved from them or their immediate progeny. Certain of these animals were later found to have scrapie in Ohio and Tennessee. During the same year, scrapie was diagnosed in three Illinois flocks. These flocks and exposed sheep moved from them were slaughtered.

In both Ohio and Illinois it appeared that the disease had been introduced from the Canadian flock involved in the first California outbreaks.

Indiana has had 23 infected flocks--more than any other State. The earliest case was in August 1954, and the most recent occurred in April 1959. Eight of these flocks as well as two in Alabama, two in North Carolina, and one in Missouri acquired the disease through movements of exposed sheep from one of the Indiana flocks. These 13 outbreaks in four States resulted from the movements of 322 exposed sheep into 85 flocks in 14 States, a classic example of spread. Had the remaining exposed sheep not been slaughtered, additional ones would undoubtedly have developed the disease.

It became obvious that scrapie could be neither controlled nor eradicated unless both source and infected flocks were slaughtered, and that exposed sheep moved from flocks in both categories and their immediate progeny should be slaughtered also.

Source flocks were defined as those determined, on ample evidence and after careful consultation, to be disseminating scrapie but in which animals showing symptoms of the disease could not be demonstrated.

On numerous occasions members of the industry, research workers, staff members of veterinary colleges, regulatory officials, and others met to discuss the scrapie problem and the eradication program. In addition representatives of these groups visited sheepmen and research institutions in Britain and France and consulted personally with authorities on the disease.

Regulatory officials and others observed that scrapie was spread over great distances through the normal movements of sheep and that, in the absence of such movement, it did not seem to spread readily through an area. This was borne out by the fact that in the instance mentioned previously the disease had spread through movements from one infected flock into 13 others in four States. In another instance one flock disseminated the disease into six flocks in two States, while sheep from two other flocks carried the disease into ten flocks in four States.

It was with this background in mind that the State-Federal Scrapie Eradication Program was broadened in April 1957, to include slaughter of source as well as infected flocks and exposed sheep moved from both source and infected flocks and their immediate progeny. Several States had previously found it necessary to adopt these procedures and had done so.

Scrapie in Other Countries

Scrapie has been known in Great Britain and Western Europe for more than 200 years. The disease has been reported in Australia, Austria, Canada, England, France, Germany, Hungary, Iceland (where a similar disease is called Rida), New Zealand, Norway, Poland (Prussia), Scotland, Spain, and Wales.

Regulatory officials in this country have worked closely with those in Canada as their scrapie problems are similar and are interfused.

In August 1959, the Canadian Scrapie Eradication Program was similarly broadened so that Canada and the United States now have equivalent programs for eradicating scrapie. This leaves a time factor discrepancy although trace-backs in both countries extended for some time prior to the dates mentioned. In order to overcome any danger inherent in this time lag, Canadian officials have given assurance that sheep which would have been slaughtered under the current program, had that program been in effect in April 1957, will not be certified for export to the United States.

Australia and New Zealand--where it is believed scrapie had been newly introduced by imported sheep--instituted an eradication program including quarantine and slaughter procedures. We understand that officials in both countries believe their efforts to eradicate scrapie have been successful. We understand also that the one outbreak among imported sheep in Norway is being similarly handled.

In certain countries where scrapie is endemic, owners attempt to reduce the incidence of the disease and the stigma of having an infected flock by slaughtering selected animals of certain bloodlines. These do not represent organized efforts to eradicate the disease.

Studies of Scrapie Outbreaks in the United States

Each outbreak is carefully studied in an attempt to establish the epidemiology of the disease. Particular attention is given to symptoms, laboratory findings, age, sex, breed, history and pedigree of each infected animal, movements from infected flocks, and the possible source of the outbreak.

During the 7 years the eradication program has been in effect in this country, it has not been possible to identify the source of a few outbreaks. However, the majority fall into a pattern and indicate spread from a limited number of common foci. Such foci--usually identified as source flocks-- are now being eliminated.

Approximately 80 percent of the infected sheep in this country were imported sheep and/or the immediate progeny of sheep of foreign registry. The broadened Canadian eradication program should materially reduce the possibility for further introduction of scrapie through sheep imported from Canada.

Exposed sheep moved from infected and source flocks and/or their immediate progeny have been removed to slaughter from some 1,700 flocks. There is no evidence that removal of these sheep only has resulted in any subsequent outbreaks of scrapie in sheep left in the flocks. The time factor involved in some flocks has been more than 7 years. In others less time has elapsed.

Presently, approximately 1,300 such flocks are receiving the required 6 months inspection. In November 1956, more than 2,000 flocks were under surveillance. These routine inspections have been quite helpful in locating infected animals. Almost 50 percent of the 88 outbreaks were found in this manner, many issuing from the period when source flocks and exposed sheep moved from infected or source flocks and their immediate progeny were inspected rather than slaughtered.

Veterinary practitioners have played an important part in locating outbreaks and reported almost one-third of the 88 infected flocks.

Two of the outbreaks were disclosed when infected sheep were shipped to market where alert Federal inspectors at public stockyards observed symptoms and suspected scrapie.

Owners have been cooperative and in many instances have reported evidence of the disease in their sheep. Sheepmen who were familiar with scrapie symptoms as a result of public meetings and veterinary inspections of their flocks notified officials of suspicious symptoms or took sheep to veterinary institutions.

Sheep less than 18 months of age seldom show symptoms of natural scrapie. Only one of the 158 infected sheep in this country was 18 months old. The others were older. Three were more than 90 months old. The great majority were from 30 to 48 months old with most being about 36 months of age.

Sheep showed symptoms of scrapie at varying periods following most recent probable exposure. Three had been away from the flocks where they are believed to have acquired the disease for periods of 41, 42, and 43 months when symptoms were noticed.

How serious a disease is scrapie? How many sheep will die of scrapie in an infected flock? Losses vary. In this country the mortality in larger flocks has been relatively low, although in one purebred flock of 500 sheep, 16 were found to have scrapie during a period of 3 or 4 months, and in another purebred flock of 174 sheep, 12 were infected. Large commercial flocks have had fewer cases.

In small purebred flocks, the mortality has been relatively higher. In some only one or two animals had the disease. In others from 5 to 36 percent of the flock showed symptoms. When an outbreak occurs, the entire flock is slaughtered before

additional cases have time to appear, thus it is not possible to determine with certainty what the losses would have been had the disease been allowed to run its course.

We are told that in countries where scrapie is endemic losses may remain at one or two animals per year, or may reach 20 to 30 percent of the flock. In one experimental group of selected sheep, natural cases have occurred in 67 percent of the lamb crop. Authorities indicate that in "infected areas" 2 to 10 percent of the sheep in perhaps 5 percent of the flocks may die of the disease.

Any discussion of scrapie usually raises the question of sheep breeds and breed susceptibility. History suggests that Spanish Merino sheep may have carried the disease into European countries many years ago. Scrapie is believed presently to exist among Merino sheep in Spain.

French veterinarians tell us that in France the disease is not limited to any one breed but occurs in several. They have developed their own breeds and do not have those from Great Britain.

Of the 158 confirmed cases in the United States, 149 were Suffolk sheep and 9 were Cheviots. Cases in Canada--where the first known outbreak of scrapie in North America occurred in 1939--have been more evenly divided between these two breeds. One infected Canadian flock consisted of both purebred Suffolk and purebred Hampshire sheep. The clinical diagnosis of scrapie in both breeds was confirmed by laboratory examination of tissues. In another Canadian flock of purebred Suffolk and purebred Southdown sheep, the disease was similarly confirmed in sheep of both breeds. Although in the United States where the majority of the cases have occurred in one breed, it is generally believed that any breed of sheep can develop the disease.

The manner in which scrapie spreads is not well understood. Both experimental and field evidence suggest that scrapie can spread from the dam, and perhaps the sire, to the progeny. Breeders who have had experience with the disease believe this to be true. In this country the pedigrees of infected sheep are carefully studied and bloodlines traced. The frequently recurring relationships observed in these studies seem too striking to be entirely coincidental. However, it is not possible to draw firm conclusions at this time. This may be possible when carefully controlled research, now underway in Great Britain, has been completed.

Although the theory that scrapie is spread from parent to offspring has many advocates, it does not fully explain the spread in certain flocks. Neither does it elucidate the means by which the disease spreads from one purebred breed to another, which appears to have been the case in two Canadian flocks where both Hampshire and Southdown sheep as well as Suffolks developed scrapie.

In England, not many years ago, the Suffolk breed was said to be free of the disease. This is obviously no longer true. There are other examples of spread from breed to breed. In the absence of crossing one breed with another, such spread is difficult to explain except by contact transmission. There may, of course, be instances of certain breeds being crossed with others; however, the characteristic appearance of some breeds makes their crossbreeding unlikely.

SUMMARY

The 88 outbreaks in the United States illustrate the potential danger of an insidious disease like scrapie in a country such as ours where lively trade among growers results in wide distribution of sheep and their diseases.

We look forward to additional research results particularly those designed to explain natural transmission. Precise information in this regard will permit more exact identification of potentially dangerous animals and, it is hoped, provide for effective eradication procedures necessitating the slaughter of fewer sheep. This knowledge is especially important in the absence of a diagnostic test.

We cannot look into a crystal ball and foretell what will happen during the next few years, but experience is convincing. The elimination of infected and exposed animals has effectively controlled the disease, prevented it from becoming widely established in Cheviot and Suffolk sheep, and has prevented spread into other breeds.

The chances for ultimate success appear good if we continue to follow sound eradication procedures and are supported by ample research.

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